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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,812	09/07/2001	Lan-Qing Huang	L0461.70115US00	3475

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EXAMINER	
DAVIS, MINH TAM B	
ART UNIT	**PAPER NUMBER**
1642	
MAIL DATE	**DELIVERY MODE**
11/16/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/856,812	HUANG ET AL.	
	Examiner	Art Unit	
	MINH-TAM DAVIS	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,9-11,42-49 and 51-55* is/are pending in the application.

4a) Of the above claim(s) *10 and 51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,9,11,42-50 and 52-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant adds new claim 55.

Accordingly, claims 1-2, 4-5, 9, 11, 42-50, 52-55, SEQ ID NO:42, or a nonapeptide comprising an unbroken sequence of SEQ ID NO:1, wherein the amino acid adjacent to the N-terminal amino acid is L and the N-terminal amino acid is L, or I are being examined.

Withdrawn Rejection

The following rejections have been withdrawn in view of the amendment: 1) 112, second paragraph, and 2) 102 rejection.

Claim Rejections - 35 USC § 112, First Paragraph, Enablement

Claims 1-2, 4-5, 9, 11, 42-50, 52-55 remain rejected under 112, first paragraph, for lack of enablement for 1) A polypeptide comprising an unbroken sequence of SEQ ID NO:1, that complexes with HLA-A2, or that elicits an immune response, 2) A nonapeptide comprising an unbroken sequence of SEQ ID NO:1, wherein the amino acid adjacent to the N-terminal amino acid is L and the N-terminal amino acid is L, or I, or a polypeptide of up to about 93 amino acids in length, and comprising said nonapeptide, and 3) A nonapeptide comprising SEQ ID NO:42, for reasons already of record in paper of 06/14/07.

The response asserts that the claimed peptides can be used for producing antibodies and CTLs, and that Example 5 shows that allogeneic tumor cell lines derived from two different melanoma patients, which cell lines were shown to express MAGE-10, are recognized by the CTLs (CTL 447A/5) provided in the instant application.

Regarding the predictability of expression of MAGE-10 (SEQ ID NO:1), the response asserts that the peptides were isolated based on recognition by a CTL clone from a melanoma patient, which means that MAGE-A10 protein must have been expressed and one or more peptides presented by the patient's immune system. The response asserts that the subject from whom the CTL clone was isolated had a primary tumor, melanoma. The response asserts that the CTLs recognize presented peptides from the expressed MAGE-A10 protein; given that MAGE-A10 is not expressed in normal tissues, normal tissues would not have produced the MAGE-A 10 protein. The response asserts that therefore, even given the teachings in the art, one skilled in the art would recognize that the data in the specification support that MAGE-A 10 is in fact expressed on primary tumor tissues. The response asserts that the RT-PCR data found in Example 6 support and confirm that view. that view. The response asserts that any further confirmation of the expression of MAGE-A10 on primary tumors could be done with routine experimentation, such as by immunohistochemistry or other antibody-based detection method, which are very well known in the art.

The response has been considered but is not found to be persuasive for the following reasons:

One cannot predict that the antibodies produced by the claimed peptides could be used for detecting cancer, because one cannot predict that the protein MAGE-10 (SEQ ID NO:1) is overexpressed in cancer in sufficient quantity such that it could be detected by its antibodies, in view of the teaching of De Plaen et al, of record, that as detected by PCR, MAGE-10 mRNA expression in various tumors is **very weak**, representing less than 1% of that of highly expressed gene. Although the specification discloses in Example 6 on Table 2 that various cancers show

expression of MAGE-10 by RT-PCR, the levels of the detected mRNAs are not disclosed. Further, it is noted that RT-PCR is very sensitive, as compared to common methods of detection by antibodies.

Concerning the claimed peptides for making CTLs, only the nonapeptide SEQ ID NO:42 as claimed in claim 9, is shown to elicit CTL response from the cell line CTL 447A/5 (the instant specification, p.32, second paragraph). Although the peptide SEQ ID NO:42 is recognized by the CTL cell line CTL447A15, there is **no indication**, nor any objective evidence that the CTL cell line CTL447A15 recognizes and **lyse any primary cancer cells**. The only cells that could stimulate CTL447A15 are the **cell lines** expressing MAGE-10 and derived from melanoma patients (the instant application, Example 5 on page 33, and the COS-7 cells transfected with MAGE-10 and artificially over-expressing MAGE-10. One cannot predict that primary cancer cells overexpress MAGE-10, based on the cell lines, because: 1) Expression of genes in cancer cells in culture is not predictably the same as that of primary cancer cells, due to the well known cell culture artifact (see Drexler et al, Embleton et al, Hsu et al, Tian et al, Van Dyke et al, Zaslav et al, and Kunkel et al, all of record), and 2) De Plaen et al, of record, teach that as detected by PCR, MAGE-10 mRNA expression in various tumors is **very weak**, representing less than 1% of that of highly expressed gene.

Concerning the CTL clone CTL447A15 generated in the instant application, the clone is generated by incubating PBL of the melanoma patient LB1751 with the irradiated LB1751-MEL **cell line** derived from said patient (Example 1, page 28). In other words, the antigens provided for stimulating the PBL for making the CTL clones are from a cell line, the expression of the genes of which is not predictably the same as that of primary cancer cells. Thus, which primary

cancer cells that overexpress MAGE-10 (SEQ ID NO:1), or overexpress the unknown antigen, the shared peptide of which is recognized by the CTL clone CTL447A15, is not known nor predictable.

Concerning "The unpredictability of cancer diagnosis and treatment", the response asserts that the claims do not require cancer diagnosis or treatment. The response asserts that therefore, any unpredictability of cancer diagnosis and treatment is irrelevant to the claimed peptides.

The response further asserts that it is routine to make antibodies and CTLs.

The response has been considered but is not found to be persuasive for the following reasons:

The issue is how to use the claimed peptides. Since one cannot predict that primary cancer cells overexpress MAGE-10 (SEQ ID NO:1) in sufficient quantities for its detection by antibodies generated by the claimed peptides, or by CTLs generated by the claimed peptide SEQ ID NO:42, supra, one would not know how to use the claimed peptide, especially in view of the unpredictability of cancer diagnosis and treatment, as taught by White et al, Smith et al, Kirkin et al, all of record.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time

policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINH-TAM DAVIS whose telephone number is 571-272-0830. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SHANON FOLEY can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MINH TAM DAVIS
November 02, 2007

SHANON FOLEY
SUPERVISORY PATENT EXAMINER
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